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IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

TAKEDA PHARMACEUTICALS U.S.A., INC., Plaintiff, v. ZYDUS PHARMACEUTICALS (USA) INC. and CADILA HEALTHCARE LIMITED Defendants.	Civil Action No. _____

COMPLAINT FOR PATENT INFRINGEMENT

Plaintiff Takeda Pharmaceuticals U.S.A., Inc. ("Takeda") files this Complaint for patent infringement against Defendants Zydus Pharmaceuticals (USA) Inc. and Cadila Healthcare Limited (collectively "Zydus" or "Defendants") and, in support thereof, alleges as follows.

NATURE OF THE ACTION

1. This is an action for patent infringement under the Food and Drug and Patent Laws of the United States, U.S.C. Titles 21 and 35 respectively, arising from Zydus's submission of Abbreviated New Drug Application ("ANDA") No. 211519 (the "Zydus ANDA") to the United States Food and Drug Administration ("FDA"), seeking approval to sell commercially a generic version of the drug product Colcrys® (colchicine, USP) (the "ANDA Product") prior to the expiration of United States Patent Nos. 7,906,519; 7,935,731; 8,093,298; 7,964,648; 8,093,297; 7,619,004; 7,601,758; 7,820,681; 7,915,269; 7,964,647; 7,981,938; 8,093,296; 8,097,655; 8,415,395; 8,415,396; 8,440,721; and 8,440,722, which cover, *inter alia*, methods of using colchicine for treating and preventing gout flares and treating Familial Mediterranean Fever.

THE PARTIES

2. Takeda Pharmaceuticals U.S.A., Inc. is a Delaware corporation with its principal place of business at One Takeda Parkway, Deerfield, IL 60015. Takeda holds all right, title, and interest in each patent asserted in this action.

3. On information and belief, Defendant Zydus Pharmaceuticals (USA) Inc. ("Zydus Inc.") is a corporation organized and existing under the laws of New Jersey, having its principal place of business at 73 Route 31 North, Pennington, New Jersey 08534.

4. On information and belief, Defendant Cadila Healthcare Limited ("Cadila") is a company organized and existing under the laws of India, having a principal place of business at Zydus Tower, Satellite Cross Roads, Ahmedabad-380015, Gujarat, India.

5. On information and belief, Zydus Inc. markets, distributes, sells, and/or offers for sale generic drugs throughout the United States and in New Jersey at the direction of, under the control of, in concert with, and for the direct benefit of Cadila.

6. On information and belief, Zydus Inc. is a wholly-owned subsidiary of Cadila.

7. On information and belief, following any FDA approval of ANDA No. 211519, Cadila will manufacture Zydus's ANDA Product for sale throughout the United States and within New Jersey. On information and belief, Cadila will do so at the direction of, under the control of, in concert with, and for the direct benefit of Zydus Inc.

8. On information and belief, Cadila assisted in the preparation and submission of ANDA No. 211519, which was done at the direction of, under the control of, in concert with, and for the direct benefit of Zydus Inc.

9. On information and belief, following any FDA approval of ANDA No. 211519, Zydus Inc. and Cadila will act in concert to market, distribute, offer for sale, and sell Zydus's ANDA Product throughout the United States and within New Jersey.

JURISDICTION AND VENUE

10. This action for patent infringement arises under 35 U.S.C. § 271.

11. This Court has subject matter jurisdiction over this matter pursuant to 28 U.S.C. §§ 1331 and 1338(a), and the Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202.

12. This Court has personal jurisdiction over Zydus Inc. and Cadila under New Jersey Rule of Court 4:4–4 and/or Fed. R. Civ. P. 4(k)(2).

13. On information and belief, Defendants regularly do or solicit business in New Jersey, engage in other persistent courses of conduct in New Jersey, and/or derive substantial revenue from products used, sold, or consumed in New Jersey, demonstrating that Defendants have continuous and systematic contacts with New Jersey.

14. On information and belief, Defendants are in the business of manufacturing and selling generic pharmaceutical products that are distributed throughout the United States, including in the State of New Jersey. On information and belief, Defendants, directly or through

their affiliates and agents, formulate, manufacture, package, market, and/or sell pharmaceutical products throughout the United States and in this judicial district.

15. Zydus Inc. filed ANDA No. 211519 with the FDA for Zydus's ANDA Product, which, on information and belief, will be manufactured by Cadila, which indicates Defendants' intention to engage in the commercial manufacture, use, offer for sale, sale, and/or importation of Zydus's ANDA Product in the United States, including in New Jersey. *See Acorda Therapeutics Inc. v. Mylan Pharm. Inc.*, 817 F.3d 755, 759-60 (Fed. Cir. 2016), *cert. denied sub nom. Mylan Pharm. v. Acorda Therapeutics*, 137 S. Ct. 625 (2017).

16. On information and belief, if ANDA No. 211519 is approved, Defendants will market, distribute, offer for sale, and/or sell Zydus's ANDA Product in the United States, including in New Jersey, and will derive substantial revenue from the use or consumption of Zydus's ANDA Product in the State of New Jersey. On information and belief, if ANDA No. 211519 is approved, Zydus's ANDA Product will be marketed, distributed, offered for sale, and/or sold in New Jersey; prescribed by physicians practicing in New Jersey; dispensed by pharmacies located within New Jersey; and/or used by patients in New Jersey, all of which will have a substantial effect on New Jersey.

17. On information and belief, Zydus Inc. is licensed to sell generic pharmaceutical products in the State of New Jersey, either directly or through one or more of its wholly owned subsidiaries, agents, and/or alter egos.

18. If ANDA No. 211519 is approved, Takeda will be harmed by Defendants' marketing, distribution, offer for sale, and/or sale of Zydus's ANDA Product, including in New Jersey.

19. On information and belief, Zydus Inc. previously has availed itself of this forum by litigating civil actions initiated in this jurisdiction. *See, e.g., Otsuka Pharm. Co., Ltd. v. Zydus Pharm. USA Inc. and Cadila Healthcare Ltd.*, No. 1:17-cv-02754 (D.N.J. Sep. 19, 2017) (D.I. 12); *Celgene Corp. v. Zydus Pharm. (USA) Inc., Zydus Int'l Pvt. Ltd., and Cadila Healthcare Ltd.*, No. 2:17-cv-02528 (D.N.J. Aug. 7, 2017) (D.I. 19); *Valeant Pharm. Luxembourg S.A.R.L., et al. v. Zydus Pharm.(USA) Inc. and Cadila Healthcare Ltd.*, No. 3:17-cv-00449 (D.N.J. Jun. 6, 2017) (D.I. 6); *Helsinn Healthcare S.A. v. Zydus Pharm. (USA) Inc. and Cadila Healthcare Ltd.*, No. 2:16-cv-04239 (D.N.J. Sep. 12, 2016) (D.I. 23); *Astrazeneca AB, et al. v. Zydus Pharm. (USA) Inc. and Cadila Healthcare Ltd.*, No. 1:15-cv-07415 (D.N.J. Jan. 18, 2016) (D.I. 8); *Supernus Pharm., Inc. v. Zydus Pharm. (USA) Inc. and Cadila Healthcare Ltd.*, No. 2:14-cv-07272 (D.N.J. May 5, 2015) (D.I. 29). On information and belief, Zydus Inc. also has affirmatively invoked this Court's jurisdiction by asserting counterclaims in cases it has litigated in New Jersey. For example, Zydus Inc. asserted counterclaims in the cases listed above.

20. On information and belief, Cadila previously has availed itself of this forum by litigating civil actions initiated in this jurisdiction. *See, e.g., Otsuka Pharm. Co., Ltd. v. Zydus Pharm. USA Inc. and Cadila Healthcare Ltd.*, No. 1:17-cv-02754 (D.N.J. Sep. 19, 2017) (D.I. 12); *Celgene Corp. v. Zydus Pharm. (USA) Inc., Zydus Int'l Pvt. Ltd., and Cadila Healthcare Ltd.*, No. 2:17-cv-02528 (D.N.J. Aug. 7, 2017) (D.I. 19); *Valeant Pharm. Luxembourg S.A.R.L., et al. v. Zydus Pharm.(USA) Inc. and Cadila Healthcare Ltd.*, No. 3:17-cv-00449 (D.N.J. Jun. 6, 2017) (D.I. 6); *Helsinn Healthcare S.A. v. Zydus Pharm. (USA) Inc. and Cadila Healthcare Ltd.*, No. 2:16-cv-04239 (D.N.J. Sep. 12, 2016) (D.I. 23); *Astrazeneca AB, et al. v. Zydus Pharm. (USA) Inc. and Cadila Healthcare Ltd.*, No. 1:15-cv-07415 (D.N.J. Jan. 18, 2016) (D.I. 8); *Supernus Pharm., Inc. v. Zydus Pharm. (USA) Inc. and Cadila Healthcare Ltd.*, No. 2:14-cv-

07272 (D.N.J. May 5, 2015) (D.I. 29). On information and belief, Cadila also has affirmatively invoked this Court's jurisdiction by asserting counterclaims in cases it has litigated in New Jersey. For example, Cadila asserted counterclaims in the cases listed above.

21. Venue is proper in this District under 28 U.S.C. § 1400(b) and/or 28 U.S.C. § 1391(b) and/or (c).

STATEMENT OF FACTS RELEVANT TO ALL COUNTS

22. Takeda is the holder of New Drug Application ("NDA") Nos. 22-351, 22-352, and 22-353, pursuant to which the FDA granted approval in 2009 for the commercial manufacturing, marketing, sale, and use of Colcrys® (colchicine, USP) tablets, 0.6 mg, pursuant to section 505(b) of the Federal Food Drug and Cosmetics Act ("FFDCA"), 21 U.S.C. § 355(b).

23. Colcrys® is primarily used to prevent and treat gout flares. Gout is a type of severe arthritis typically characterized by extremely painful "flares" (severe and sudden attacks of pain, redness, inflammation, and tenderness in joints) resulting from a build-up of uric acid. Colcrys® and Takeda's authorized generic of Colcrys® are the only oral single-active-ingredient colchicine products approved by the FDA for the treatment and prevention of gout flares.

24. Colcrys® is also used to treat Familial Mediterranean Fever ("FMF"). FMF is a rare, autosomal recessive, auto-inflammatory disease characterized by recurrent and/or chronic inflammation. Colcrys® and Takeda's authorized generic of Colcrys® are the only single-active-ingredient oral colchicine products currently on the market to treat FMF.

25. As part of the FDA approval for Colcrys®, Takeda received Orphan Drug exclusivity, which expired July 29, 2016.

26. At the time the FDA granted approval to Colcrys® in 2009, the NDA holder was Takeda's predecessor-in-interest, Mutual Pharmaceutical Company, Inc. ("Mutual"). Mutual conducted groundbreaking research, discovering important new information about colchicine,

including previously unknown information concerning safety and efficacy, tolerability, dangerous side effects, and interactions with other medicines and substances.

27. Before Colcrys®, no oral single-ingredient colchicine had been reviewed by the FDA for safety and efficacy. The lack of FDA-reviewed data regarding oral single-ingredient colchicine was particularly troublesome because colchicine is potentially toxic. Before Mutual introduced Colcrys®, oral colchicine had been associated with more than 160 deaths. Accordingly, to support the safe and effective use of an oral single-ingredient colchicine product, Mutual developed its own formulation and studied the effects of that formulation in human subjects.

28. One of Mutual's clinical studies, the Acute Gout Flare Receiving Colchicine Evaluation ("AGREE") trial, provided important new information on the optimal dose of colchicine for treatment of gout flares. Traditionally, oral colchicine had been used for the treatment of gout flares by administering an initial dose of one to two 0.6 mg tablets at the onset of the flare, followed by additional doses every one to two hours until either the pain subsided or "nausea, vomiting, or diarrhea" developed. Many patients following this regimen would take a total dose of up to 8 mg of colchicine, which frequently led to toxicity-related side effects such as diarrhea or vomiting.

29. The AGREE trial completely upended the conventional wisdom. The trial was a double-blind, placebo-controlled, multicenter, dose-comparison study involving 575 trial participants. It compared the effects of the "traditional" dose described above to a lower dose of just 1.8 mg total of colchicine, administered as 1.2 mg colchicine followed by 0.6 mg 1 hour later. The AGREE trial proved that the lower-dose regimen is just as effective as the traditional higher-dose regimen but without the serious adverse events of the higher dose. Based on

Mutual's trial, the FDA approved Mutual's colchicine product with the low-dose regimen as safe and effective for the treatment of gout flares. The Colcrys® low-dose regimen is recited in the FDA-approved product label attached as Exhibit A.

30. In 2012, the American College of Rheumatology ("ACR") issued guidelines for management of gout. The ACR guidelines adopt Takeda's low-dose regimen. The ACR recommends treating an acute gout flare by using a loading dose of 1.2 mg of colchicine, followed by 0.6 mg 1 hour later, and then, 12 hours later, resuming 0.6 mg prophylactic dosing once or twice daily, unless dose adjustment is necessary. The ACR recommendation remains the standard of care for the use of colchicine to treat acute gout flares. Part II of the ACR guidelines, addressing therapy and prophylaxis of acute gouty arthritis, is attached as Exhibit B. *See* Ex. B at 1453.

31. Mutual also conducted multiple studies regarding potential adverse drug interactions involving colchicine. Mutual researched numerous drug interactions that could result in unsafe levels of colchicine and even death. Mutual discovered, for example, that co-administering colchicine with clarithromycin could increase colchicine blood levels by nearly 230%, creating a risk of toxicity. Mutual identified potentially dangerous interactions between colchicine and several other drugs, and it recommended colchicine dosing reductions to reduce the risk of an adverse reaction when colchicine is administered concomitantly with such other drugs. This dose adjustment information is currently included in the approved labeling for Colcrys®, which specifies appropriate dose adjustments when Colcrys® is co-administered with ketoconazole, verapamil, ritonavir, clarithromycin, and other drugs. *See, e.g.*, Ex. A at Table 1; *see also* Ex. B at 1453 (ACR Guidelines recommending dose adjustments in Colcrys labeling).

TAKEDA'S COLCRYS® PATENTS

32. Takeda is the lawful owner of all right, title, and interest in and to the following United States patents, including the right to sue and to recover for infringement thereof, which contain one or more claims covering methods of using Colcrys®.

A. United Sates Patent Number 7,906,519 ("the '519 Patent"), entitled "METHODS FOR CONCOMITANT ADMINISTRATION OF COLCHICINE AND A SECOND ACTIVE AGENT," a copy of which is attached hereto as Exhibit C and incorporated herein by reference as though set forth in full, which was duly and legally issued March 15, 2011, naming Matthew Davis as the inventor.

B. United States Patent Number 7,935,731 ("the '731 Patent"), entitled "METHODS FOR CONCOMITANT ADMINISTRATION OF COLCHICINE AND MACROLIDE ANTIBIOTICS," a copy of which is attached hereto as Exhibit D and incorporated herein by reference as though set forth in full, which was duly and legally issued May 3, 2011, naming Matthew Davis as the inventor.

C. United States Patent Number 8,093,298 ("the '298 Patent"), entitled "METHODS FOR CONCOMITANT ADMINISTRATION OF COLCHICINE AND MACROLIDE ANTIBIOTICS," a copy of which is attached hereto as Exhibit E and incorporated herein by reference as though set forth in full, which was duly and legally issued January 10, 2012, naming Matthew Davis as the inventor.

D. United States Patent Number 7,964,648 ("the '648 Patent"), entitled "METHODS FOR CONCOMITANT ADMINISTRATION OF COLCHICINE AND A SECOND ACTIVE AGENT," a copy of which is attached hereto as Exhibit F and incorporated herein by reference as though set forth in full, which was duly and legally issued June 21, 2011, naming Matthew Davis as the inventor.

E. United States Patent Number 8,093,297 ("the '297 Patent"), entitled "METHODS FOR CONCOMITANT ADMINISTRATION OF COLCHICINE AND A SECOND ACTIVE AGENT," a copy of which is attached hereto as Exhibit G and incorporated herein by reference as though set forth in full, which was duly and legally issued January 10, 2012, naming Matthew Davis as the inventor.

F. United States Patent Number 7,619,004 ("the '004 Patent"), entitled "METHODS FOR CONCOMITANT ADMINISTRATION OF COLCHICINE AND MACROLIDE ANTIBIOTICS," a copy of which is attached hereto as Exhibit H and incorporated herein by reference as though set forth in full, which was duly and legally issued November 17, 2009, naming Matthew Davis as the inventor.

G. United States Patent Number 7,601,758 ("the '758 Patent"), entitled "METHODS FOR CONCOMITANT ADMINISTRATION OF COLCHICINE AND MACROLIDE ANTIBIOTICS IN THE TREATMENT OF GOUT FLARES," a copy of which is attached hereto as Exhibit I and incorporated herein by reference as though set forth in full, which was duly and legally issued October 13, 2009, naming Matthew Davis as the inventor.

H. United States Patent Number 7,820,681 ("the '681 Patent"), entitled "METHODS FOR CONCOMITANT ADMINISTRATION OF COLCHICINE AND A SECOND ACTIVE AGENT," a copy of which is attached hereto as Exhibit J and incorporated herein by reference as though set forth in full, which was duly and legally issued October 26, 2010, naming Matthew Davis as the inventor.

I. United States Patent Number 7,915,269 ("the '269 Patent"), entitled "METHODS FOR CONCOMITANT ADMINISTRATION OF COLCHICINE AND A SECOND ACTIVE AGENT," a copy of which is attached hereto as Exhibit K and incorporated

herein by reference as though set forth in full, which was duly and legally issued March 29, 2011, naming Matthew Davis as the inventor.

J. United States Patent Number 7,964,647 ("the '647 Patent"), entitled "COLCHICINE COMPOSITIONS AND METHODS," a copy of which is attached hereto as Exhibit L and incorporated herein by reference as though set forth in full, which was duly and legally issued June 21, 2011, naming Matthew Davis as the inventor.

K. United States Patent Number 7,981,938 ("the '938 Patent"), entitled "COLCHICINE COMPOSITIONS AND METHODS," a copy of which is attached hereto as Exhibit M and incorporated herein by reference as though set forth in full, which was duly and legally issued July 19, 2011, naming Matthew Davis as the inventor.

L. United States Patent Number 8,093,296 ("the '296 Patent"), entitled "METHODS FOR CONCOMITANT ADMINISTRATION OF COLCHICINE AND MACROLIDE ANTIBIOTICS," a copy of which is attached hereto as Exhibit N and incorporated herein by reference as though set forth in full, which was duly and legally issued January 10, 2012, naming Matthew Davis as the inventor.

M. United States Patent Number 8,097,655 ("the '655 Patent"), entitled "METHODS FOR CONCOMITANT ADMINISTRATION OF COLCHICINE AND MACROLIDE ANTIBIOTICS," a copy of which is attached hereto as Exhibit O and incorporated herein by reference as though set forth in full, which was duly and legally issued January 17, 2012, naming Matthew Davis as the inventor.

N. United States Patent Number 8,415,395 ("the '395 Patent"), entitled "COLCHICINE COMPOSITIONS AND METHODS," a copy of which is attached hereto as

Exhibit P and incorporated herein by reference as though set forth in full, which was duly and legally issued April 9, 2013, naming Matthew Davis and Hengsheng Feng as inventors.

O. United States Patent Number 8,415,396 ("the '396 Patent"), entitled "COLCHICINE COMPOSITIONS AND METHODS," a copy of which is attached hereto as Exhibit Q and incorporated herein by reference as though set forth in full, which was duly and legally issued April 9, 2013, naming Matthew Davis and Hengsheng Feng as inventors.

P. United States Patent Number 8,440,721 ("the '721 Patent"), entitled "METHODS FOR CONCOMITANT ADMINISTRATION OF COLCHICINE AND A SECOND ACTIVE AGENT," a copy of which is attached hereto as Exhibit R and incorporated herein by reference as though set forth in full, which was duly and legally issued May 14, 2013, naming Matthew Davis as the inventor.

Q. United States Patent Number 8,440,722 ("the '722 Patent"), entitled "METHODS FOR CONCOMITANT ADMINISTRATION OF COLCHICINE AND A SECOND ACTIVE AGENT," a copy of which is attached hereto as Exhibit S and incorporated herein by reference as though set forth in full, which was duly and legally issued May 14, 2013, naming Matthew Davis as the inventor.

33. The '519, '731, '298, '648 and '297 Patents are collectively referred to herein as the "FMF Patents."

34. The '004, '758, '681, '269, '647, '648, '938, '296, '297, '655, '395, '396, '721, and '722 Patents are collectively referred to herein as the "Gout Patents." (The '648 and '297 patents are both FMF Patents and Gout Patents.)

35. The '647, '938, '395, and '396 Patents are collectively referred to herein as the "Acute Gout Flare Patents."

36. The ’519, ’731, ’298, ’648, ’297, ’004, ’758, ’681, ’269, ’648, ’296, ’297, ’655, ’721, and ’722 Patents are collectively referred to herein as the “Drug-Drug Interaction” or “DDI Patents.”

37. All of the above-listed patents are collectively referred to herein as the “Colcrys® Patents.”

38. The Colcrys® Patents are listed in the FDA’s “Approved Drug Products with Therapeutic Equivalence Evaluations” (commonly referred to as the “Orange Book”) as patents “with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug.” 21 U.S.C. § 355(b)(1).

DEFENDANTS’ ACTIONS GIVING RISE TO THIS SUIT

39. Zydus Inc. submitted ANDA No. 211519 to the FDA seeking approval to engage in the commercial use, manufacture, sale, offer for sale, or importation of 0.6 mg oral colchicine tablets (i.e., Zydus’s ANDA Product) prior to the expiration of Takeda’s patents relating to Colcrys®.

40. On information and belief, following any FDA approval of ANDA No. 211519, Cadila will manufacture Zydus’s ANDA Product for sale throughout the United States and within Delaware.

41. On or about February 19, 2018, Takeda received a letter dated February 15, 2018, notifying Takeda of Zydus Inc.’s submission to the FDA of ANDA No. 211519, seeking approval to engage in the commercial use, manufacture, sale, offer for sale, or importation of Zydus’s ANDA Product and containing a certification under 21 U.S.C. § 355(j)(2)(A)(vii)(IV) (“Paragraph IV Certification”) with respect to all 17 of the Colcrys® Patents (hereinafter, the “Paragraph IV Notice Letter”). Zydus Inc. asserted in its Paragraph IV Notice Letter that it is

entitled to bring its product to market prior to the expiration of Takeda's Colcrys® Patents because no valid claim of the Colcrys® Patents would be infringed by the manufacture, use, or sale of the Zydus ANDA Product.

42. Zydus Inc.'s Paragraph IV Notice Letter included "Zydus's Detailed Factual and Legal Bases in Support of its Paragraph IV Certification for Colchicine Tablets, 0.6 mg." Zydus Inc's Paragraph IV Notice Letter set forth Zydus Inc.'s positions regarding the invalidity of the Colcrys® Patents.

43. Zydus Inc.'s Paragraph IV Notice Letter also included an offer to the patentee of confidential access pursuant to 21 U.S.C. § 355(G)(5)(C). Takeda accepted Zydus Inc.'s offer of confidential access, and counsel for Takeda reviewed portions of Zydus Inc.'s ANDA No. 211519 before bringing this infringement action.

44. Takeda commenced this action within 45 days of receiving Zydus Inc.'s Paragraph IV Notice Letter.

DEFENDANTS' INFRINGEMENT OF THE COLCRYS® PATENTS

45. Takeda's FDA-approved product label for Colcrys® teaches and encourages, *inter alia*, methods of using Colcrys® claimed in the Colcrys® Patents, including the use of colchicine to treat gout or FMF when a patient is or is not taking another substance. *See*, *e.g.*, Ex. A at Table 1.

46. Under the FFDCA, drug products submitted to the FDA for approval via an ANDA are required to have the same labeling as the reference listed drug, here Colcrys®, except for changes required because of differences approved under a suitability petition (21 U.S.C. § 355(j)(2)(C); 21 C.F.R. § 314.93), because the generic drug product and reference listed drug are produced or distributed by different manufacturers (21 U.S.C. § 355(j)(2)(A)(v); 21 C.F.R.

§314.94(a)(8)(iv)), or because the ANDA applicant has made a section viii carve-out for one of the indications on the label of the reference listed drug.

47. The approved labeling for Colcrys® recites the claimed methods of Takeda's Colcrys® Patents.

48. The Colcrys® labeling states:

> The recommended dose of COLCRYS for treatment of a gout flare is 1.2 mg (two tablets) at the first sign of the flare followed by 0.6 mg (one tablet) one hour later. Higher doses have not been found to be more effective. The maximum recommended dose for treatment of gout flares is 1.8 mg over a one-hour period. COLCRYS may be administered for treatment of a gout flare during prophylaxis at doses not to exceed 1.2 mg (two tablets) at the first sign of the flare followed by 0.6 mg (one tablet) one hour later. Wait 12 hours and then resume the prophylactic dose.

Ex. A at § 2.1. The Colcrys® labeling recites the claimed methods of Takeda's Acute Gout Flare Patents. For example, claim 1 of the '647 patent recites:

> A method of treating a patient having an acute gouty arthritis attack with colchicine consisting of
>
> administering 1.2 mg oral colchicine to a human patient having an acute gouty arthritis attack at the onset of the acute gouty arthritis attack, followed by 0.6 mg oral colchicine one hour later.

Ex. L at claim 1.

49. The Colcrys® labeling also states that "[c]o-administration of COLCRYS with drugs known to inhibit CYP3A4 and/or P-glycoprotein (P-gp) increases the risk of colchicine-induced toxic effects (Table 1). If patients are taking or have recently completed treatment with drugs listed in Table 1 within the prior 14 days, the dose adjustments are as shown on the table below [see DRUG INTERACTIONS (7)]." *See* Ex. A § 2.4; *see also id.* § 7 ("Table 1 provides recommendations for strong and moderate CYP3A4 inhibitors and P-gp inhibitors."). Table 1 is reproduced in part below:

Table 1
COLCRYS Dose Adjustment for Co-administration with Interacting Drugs if no Alternative Available[1]

Strong CYP3A4 Inhibitors[2]							
Drug	**Noted or Anticipated Outcome**	**Gout Flares**				**FMF**	
		Prophylaxis of Gout Flares		**Treatment of Gout Flares**			
		Original Intended Dosage	**Adjusted Dose**	**Original Intended Dosage**	**Adjusted Dose**	**Original Intended Dosage**	**Adjusted Dose**
Atazanavir Clarithromycin Darunavir/ Ritonavir[3] Indinavir Itraconazole Ketoconazole Lopinavir/ Ritonavir[3] Nefazodone Nelfinavir Ritonavir Saquinavir Telithromycin Tipranavir/ Ritonavir[3]	Significant increase in colchicine plasma levels[1]; fatal colchicine toxicity has been reported with clarithromycin, a strong CYP3A4 inhibitor. Similarly, significant increase in colchicine plasma levels is anticipated with other strong CYP3A4 inhibitors.	0.6 mg twice a day 0.6 mg once a day	0.3 mg once a day 0.3 mg once every other day	1.2 mg (2 tablets) followed by 0.6 mg (1 tablet) 1 hour later. Dose to be repeated no earlier than 3 days.	0.6 mg (1 tablet) x 1 dose, followed by 0.3 mg (1/2 tablet) 1 hour later. Dose to be repeated no earlier than 3 days.	Maximum daily dose of 1.2 – 2.4 mg	Maximum daily dose of 0.6 mg (may be given as 0.3 mg twice a day)
Moderate CYP3A4 Inhibitors							
Drug	**Noted or Anticipated Outcome**	**Gout Flares**				**FMF**	
		Prophylaxis of Gout Flares		**Treatment of Gout Flares**			
		Original Intended Dosage	**Adjusted Dose**	**Original Intended Dosage**	**Adjusted Dose**	**Original Intended Dosage**	**Adjusted Dose**
Amprenavir[3] Aprepitant Diltiazem Erythromycin Fluconazole Fosamprenavir[3] (pro-drug of Amprenavir) Grapefruit Juice Verapamil	Significant increase in colchicine plasma concentration is anticipated. Neuromuscular toxicity has been reported with diltiazem and verapamil interactions.	0.6 mg twice a day 0.6 mg once a day	0.3 mg twice a day or 0.6 mg once a day 0.3 mg once a day	1.2 mg (2 tablets) followed by 0.6 mg (1 tablet) 1 hour later. Dose to be repeated no earlier than 3 days.	1.2 mg (2 tablets) x 1 dose. Dose to be repeated no earlier than 3 days.	Maximum daily dose of 1.2 – 2.4 mg.	Maximum daily dose of 1.2 mg (may be given as 0.6 mg twice a day)

50. The Colcrys® labeling provides dose adjustments for colchicine when coadministered with ketoconazole, verapamil, ritonavir, clarithromycin, and other drugs. These dose adjustments are disclosed and claimed in Takeda's DDI Patents. For example, claim 1 of the '298 patent recites the following:

> 1. A method of using colchicine for the treatment of Familial Mediterranean Fever in a human adult or child > 12 years of age in need of treatment thereof, said method comprising:
>
> orally administering a reduced colchicine dosage amount to the human adult or child > 12 years of age in need of treatment for Familial Mediterranean Fever who is concomitantly receiving administration of clarithromycin within 1 to 2 days of oral administration of colchicine, wherein the reduced colchicine dosage amount is

> reduced compared to a daily dosage amount to be administered in the absence of concomitant clarithromycin,
>
> wherein the daily dosage amount to be administered in the absence of concomitant clarithromycin is a maximum of 2.4 mg per day, and
>
> wherein the reduced colchicine dosage amount is a maximum of 0.6 mg per day.

See Ex. E, claim 1. The dose adjustment table in the Colcrys® labeling provides that the usual intended dose of colchicine for FMF is a maximum of 2.4 mg. When colchicine is used with a strong CYP3A4 inhibitor such as clarithromycin, the Colcrys® labeling teaches that it should be adjusted from 2.4 mg per day to a reduced colchicine dosage of 0.6 mg per day (which may be given as 0.3 mg twice per day).

51. Accordingly, on information and belief, Zydus's labeling for its ANDA Product, like the labeling for Colcrys®, recites methods of using colchicine disclosed and claimed in the Colcrys® Patents.

52. If Zydus's ANDA Product is approved by the FDA, Zydus will induce others to infringe one or more claims of the Colcrys® Patents. Specifically, Zydus's label will explicitly instruct doctors, pharmacists, other healthcare professionals, and patients to administer Zydus's ANDA Product according to methods claimed in one or more claims of the Colcrys® Patents.

53. On information and belief, Zydus's ANDA Product will be administered for the treatment and prophylaxis of acute gout flares and for the treatment of FMF.

54. On information and belief, Zydus's label demonstrates Zydus's specific intent that a doctor, pharmacist, other healthcare professional, or patient administer Zydus's ANDA Product according to the instructions on Zydus's labeling regarding treatment of acute gout flares and will thus directly infringe one or more claims of the Acute Gout Flare Patents.

55. Doctors, pharmacists, other healthcare professionals, and patients will administer Zydus's ANDA Product according to the instructions on Zydus's labeling regarding the treatment of acute gout flares and will thus infringe one or more claims of the Acute Gout Flare Patents.

56. On information and belief, Zydus's label demonstrates Zydus's specific intent that, when concomitant administration is necessary or desirable, a doctor, pharmacist, other healthcare professional, or patient administer Zydus's ANDA Product according to the instructions on Zydus's labeling regarding dose reduction during concomitant administration and thus directly infringe one or more claims of the DDI Patents.

57. On information and belief, some Gout and FMF patients will undergo concomitant treatment with colchicine for Gout and FMF and ketoconazole for a fungal infection.

58. On information and belief, some Gout and FMF patients will undergo concomitant treatment with colchicine for Gout and FMF and ritonavir for HIV or other viral infections.

59. On information and belief, some Gout and FMF patients will undergo concomitant treatment with colchicine for Gout and FMF and clarithromycin for bacterial infections, including *H. pylori*.

60. On information and belief, some Gout patients will undergo concomitant treatment with colchicine for the treatment and/or prevention of acute gout flares and verapamil for hypertension, angina pectoris, cardia arrhythmia, and/or other disorders.

61. On information and belief, patients concomitantly taking ketoconazole, ritonavir, verapamil, and/or clarithromycin with colchicine will be prescribed Zydus's ANDA Product

according to the instructions on Zydus's labeling regarding dose reductions in accordance with Takeda's DDI Patents by doctors or other healthcare professionals. Such doctors, healthcare professionals, and patients thus will directly infringe one or more claims of the DDI Patents.

EXCEPTIONAL CASE

62. On information and belief, Zydus is aware of all of the Colcrys® Patents.

63. Zydus's Paragraph IV Certification with respect to the Colcrys® Patents for ANDA No. 211519 is without adequate basis. Zydus's actions render this an exceptional case under 35 U.S.C. § 285.

COUNT I

(Infringement of the '519 Patent)

64. Paragraphs 1 to 63 are incorporated herein as set forth above.

65. Zydus has committed an act of infringement of the '519 Patent that creates a justiciable case or controversy between Takeda and Zydus.

66. Zydus's submission of its ANDA No. 211519 to seek approval to engage in the commercial use, manufacture, sale, offer for sale, or importation of Zydus's ANDA Product prior to expiration of the '519 Patent constitutes infringement of claim 1 of the '519 Patent under 35 U.S.C. § 271(e)(2)(A).

67. Unless enjoined by the Court, upon FDA approval of ANDA No. 211519, Zydus will induce infringement of the '519 Patent under 35 U.S.C. § 271(b) by making, using, importing, selling, and offering to sell Zydus's ANDA Product in the United States. On information and belief, upon approval of ANDA No. 211519, Zydus will intentionally encourage acts of direct infringement by healthcare providers administering, and/or patients using, Zydus's ANDA Product with knowledge of the '519 Patent and knowledge that its acts are encouraging infringement.

68. Takeda will be irreparably harmed by Zydus's infringing activities unless those activities are enjoined by this Court.

69. Takeda does not have an adequate remedy at law.

COUNT II

(Infringement of the '731 Patent)

70. Paragraphs 1 to 69 are incorporated herein as set forth above.

71. Zydus has committed an act of infringement of the '731 Patent that creates a justiciable case or controversy between Takeda and Zydus.

72. Zydus's submission of its ANDA No. 211519 to seek approval to engage in the commercial use, manufacture, sale, offer for sale, or importation of Zydus's ANDA Product prior to expiration of the '731 Patent constitutes infringement of claim 1 of the '731 Patent under 35 U.S.C. § 271(e)(2)(A).

73. Unless enjoined by the Court, upon FDA approval of ANDA No. 211519, Zydus will induce infringement of the '731 Patent under 35 U.S.C. § 271(b) by making, using, importing, selling, and offering to sell Zydus's ANDA Product in the United States. On information and belief, upon approval of ANDA No. 211519, Zydus will intentionally encourage acts of direct infringement by healthcare providers administering, and/or patients using, Zydus's ANDA Product with knowledge of the '731 Patent and knowledge that its acts are encouraging infringement.

74. Takeda will be irreparably harmed by Zydus's infringing activities unless those activities are enjoined by this Court.

75. Takeda does not have an adequate remedy at law.

COUNT III

(Infringement of the ’298 Patent)

76. Paragraphs 1 to 75 are incorporated herein as set forth above.

77. Zydus has committed an act of infringement of the ’298 Patent that creates a justiciable case or controversy between Takeda and Zydus.

78. Zydus’s submission of its ANDA No. 211519 to seek approval to engage in the commercial use, manufacture, sale, offer for sale, or importation of Zydus’s ANDA Product prior to expiration of the ’298 Patent constitutes infringement of one or more claims of the ’298 Patent, including at least claim 1 of the ’298 Patent, under 35 U.S.C. § 271(e)(2)(A).

79. Unless enjoined by the Court, upon FDA approval of ANDA No. 211519, Zydus will induce infringement of the ’298 Patent under 35 U.S.C. § 271(b) by making, using, importing, selling, and offering to sell Zydus’s ANDA Product in the United States. On information and belief, upon approval of ANDA No. 211519, Zydus will intentionally encourage acts of direct infringement by healthcare providers administering, and/or patients using, Zydus’s ANDA Product with knowledge of the ’298 Patent and knowledge that its acts are encouraging infringement.

80. Takeda will be irreparably harmed by Zydus’s infringing activities unless those activities are enjoined by this Court.

81. Takeda does not have an adequate remedy at law.

COUNT IV

(Infringement of the ’648 Patent)

82. Paragraphs 1 to 81 are incorporated herein as set forth above.

83. Zydus has committed an act of infringement of the ’648 Patent that creates a justiciable case or controversy between Takeda and Zydus.

84. Zydus's submission of its ANDA No. 211519 to seek approval to engage in the commercial use, manufacture, sale, offer for sale, or importation of Zydus's ANDA Product prior to expiration of the '648 Patent constitutes infringement of one or more claims of the '648 Patent, including at least claim 1 of the '648 Patent, under 35 U.S.C. § 271(e)(2)(A).

85. Unless enjoined by the Court, upon FDA approval of ANDA No. 211519, Zydus will induce infringement of the '648 Patent under 35 U.S.C. § 271(b) by making, using, importing, selling, and offering to sell Zydus's ANDA Product in the United States. On information and belief, upon approval of ANDA No. 211519, Zydus will intentionally encourage acts of direct infringement by healthcare providers administering, and/or patients using, Zydus's ANDA Product with knowledge of the '648 Patent and knowledge that its acts are encouraging infringement.

86. Takeda will be irreparably harmed by Zydus's infringing activities unless those activities are enjoined by this Court.

87. Takeda does not have an adequate remedy at law.

COUNT V

(Infringement of the '297 Patent)

88. Paragraphs 1 to 87 are incorporated herein as set forth above.

89. Zydus has committed an act of infringement of the '297 Patent that creates a justiciable case or controversy between Takeda and Zydus.

90. Zydus's submission of its ANDA No. 211519 to seek approval to engage in the commercial use, manufacture, sale, offer for sale, or importation of Zydus's ANDA Product prior to expiration of the '297 Patent constitutes infringement of one or more claims of the '297 Patent, including at least claim 1 of the '297 Patent, under 35 U.S.C. § 271(e)(2)(A).

91. Unless enjoined by the Court, upon FDA approval of ANDA No. 211519, Zydus will induce infringement of the ’297 Patent under 35 U.S.C. § 271(b) by making, using, importing, selling, and offering to sell Zydus’s ANDA Product in the United States. On information and belief, upon approval of ANDA No. 211519, Zydus will intentionally encourage acts of direct infringement by healthcare providers administering, and/or patients using, Zydus’s ANDA Product with knowledge of the ’297 Patent and knowledge that its acts are encouraging infringement.

92. Takeda will be irreparably harmed by Zydus’s infringing activities unless those activities are enjoined by this Court.

93. Takeda does not have an adequate remedy at law.

COUNT VI

(Infringement of the ’004 Patent)

94. Paragraphs 1 to 93 are incorporated herein as set forth above.

95. Zydus has committed an act of infringement of the ’004 Patent that creates a justiciable case or controversy between Takeda and Zydus.

96. Zydus’s submission of its ANDA No. 211519 to seek approval to engage in the commercial use, manufacture, sale, offer for sale, or importation of Zydus’s ANDA Product prior to expiration of the ’004 Patent constitutes infringement of one or more claims of the ’004 Patent, including at least claim 5 of the ’004 Patent under 35 U.S.C. § 271(e)(2)(A).

97. Unless enjoined by the Court, upon FDA approval of ANDA No. 211519, Zydus will induce infringement of the ’004 Patent under 35 U.S.C. § 271(b) by making, using, importing, selling, and offering to sell Zydus’s ANDA Product in the United States. On information and belief, upon approval of ANDA No. 211519, Zydus will intentionally encourage acts of direct infringement by healthcare providers administering, and/or patients using, Zydus’s

ANDA Product with knowledge of the '004 Patent and knowledge that its acts are encouraging infringement.

98. Takeda will be irreparably harmed by Zydus's infringing activities unless those activities are enjoined by this Court.

99. Takeda does not have an adequate remedy at law.

COUNT VII

(Infringement of the '758 Patent)

100. Paragraphs 1 to 99 are incorporated herein as set forth above.

101. Zydus has committed an act of infringement of the '758 Patent that creates a justiciable case or controversy between Takeda and Zydus.

102. Zydus's submission of its ANDA No. 211519 to seek approval to engage in the commercial use, manufacture, sale, offer for sale, or importation of Zydus's ANDA Product prior to expiration of the '758 Patent constitutes infringement of one or more claims of the '758 Patent, including at least claim 10 of the '758 Patent under 35 U.S.C. § 271(e)(2)(A).

103. Unless enjoined by the Court, upon FDA approval of ANDA No. 211519, Zydus will induce infringement of the '758 Patent under 35 U.S.C. § 271(b) by making, using, importing, selling, and offering to sell Zydus's ANDA Product in the United States. On information and belief, upon approval of ANDA No. 211519, Zydus will intentionally encourage acts of direct infringement by healthcare providers administering, and/or patients using, Zydus's ANDA Product with knowledge of the '758 Patent and knowledge that its acts are encouraging infringement.

104. Takeda will be irreparably harmed by Zydus's infringing activities unless those activities are enjoined by this Court.

105. Takeda does not have an adequate remedy at law.

COUNT VIII

(Infringement of the ’681 Patent)

106. Paragraphs 1 to 105 are incorporated herein as set forth above.

107. Zydus has committed an act of infringement of the ’681 Patent that creates a justiciable case or controversy between Takeda and Zydus.

108. Zydus’s submission of its ANDA No. 211519 to seek approval to engage in the commercial use, manufacture, sale, offer for sale, or importation of Zydus’s ANDA Product prior to expiration of the ’681 Patent constitutes infringement of one or more claims of the ’681 Patent, including at least claim 1 of the ’681 Patent under 35 U.S.C. § 271(e)(2)(A).

109. Unless enjoined by the Court, upon FDA approval of ANDA No. 211519, Zydus will induce infringement of the ’681 Patent under 35 U.S.C. § 271(b) by making, using, importing, selling, and offering to sell Zydus’s ANDA Product in the United States. On information and belief, upon approval of ANDA No. 211519, Zydus will intentionally encourage acts of direct infringement by healthcare providers administering, and/or patients using, Zydus’s ANDA Product with knowledge of the ’681 Patent and knowledge that its acts are encouraging infringement.

110. Takeda will be irreparably harmed by Zydus’s infringing activities unless those activities are enjoined by this Court.

111. Takeda does not have an adequate remedy at law.

COUNT IX

(Infringement of the ’269 Patent)

112. Paragraphs 1 to 111 are incorporated herein as set forth above.

113. Zydus has committed an act of infringement of the ’269 Patent that creates a justiciable case or controversy between Takeda and Zydus.

114. Zydus's submission of its ANDA No. 211519 to seek approval to engage in the commercial use, manufacture, sale, offer for sale, or importation of Zydus's ANDA Product prior to expiration of the '269 Patent constitutes infringement of claim 1 of the '269 Patent under 35 U.S.C. § 271(e)(2)(A).

115. Unless enjoined by the Court, upon FDA approval of ANDA No. 211519, Zydus will induce infringement of the '269 Patent under 35 U.S.C. § 271(b) by making, using, importing, selling, and offering to sell Zydus's ANDA Product in the United States. On information and belief, upon approval of ANDA No. 211519, Zydus will intentionally encourage acts of direct infringement by healthcare providers administering, and/or patients using, Zydus's ANDA Product with knowledge of the '269 Patent and knowledge that its acts are encouraging infringement.

116. Takeda will be irreparably harmed by Zydus's infringing activities unless those activities are enjoined by this Court.

117. Takeda does not have an adequate remedy at law.

COUNT X

(Infringement of the '647 Patent)

118. Paragraphs 1 to 117 are incorporated herein as set forth above.

119. Zydus has committed an act of infringement of the '647 Patent that creates a justiciable case or controversy between Takeda and Zydus.

120. Zydus's submission of its ANDA No. 211519 to seek approval to engage in the commercial use, manufacture, sale, offer for sale, or importation of Zydus's ANDA Product prior to expiration of the '647 Patent constitutes infringement of claim 1 of the '647 Patent under 35 U.S.C. § 271(e)(2)(A).

121. Unless enjoined by the Court, upon FDA approval of ANDA No. 211519, Zydus will induce infringement of the ’647 Patent under 35 U.S.C. § 271(b) by making, using, importing, selling, and offering to sell Zydus’s ANDA Product in the United States. On information and belief, upon approval of ANDA No. 211519, Zydus will intentionally encourage acts of direct infringement by healthcare providers administering, and/or patients using, Zydus’s ANDA Product with knowledge of the ’647 Patent and knowledge that its acts are encouraging infringement.

122. Takeda will be irreparably harmed by Zydus’s infringing activities unless those activities are enjoined by this Court.

123. Takeda does not have an adequate remedy at law.

COUNT XI

(Infringement of the ’938 Patent)

124. Paragraphs 1 to 123 are incorporated herein as set forth above.

125. Zydus has committed an act of infringement of the ’938 Patent that creates a justiciable case or controversy between Takeda and Zydus.

126. Zydus’s submission of its ANDA No. 211519 to seek approval to engage in the commercial use, manufacture, sale, offer for sale, or importation of Zydus’s ANDA Product prior to expiration of the ’938 Patent constitutes infringement of claim 1 of the ’938 Patent under 35 U.S.C. § 271(e)(2)(A).

127. Unless enjoined by the Court, upon FDA approval of ANDA No. 211519, Zydus will induce infringement of the ’938 Patent under 35 U.S.C. § 271(b) by making, using, importing, selling, and offering to sell Zydus’s ANDA Product in the United States. On information and belief, upon approval of ANDA No. 211519, Zydus will intentionally encourage acts of direct infringement by healthcare providers administering, and/or patients using, Zydus’s

ANDA Product with knowledge of the ’938 Patent and knowledge that its acts are encouraging infringement.

128. Takeda will be irreparably harmed by Zydus’s infringing activities unless those activities are enjoined by this Court.

129. Takeda does not have an adequate remedy at law.

COUNT XII

(Infringement of the ’296 Patent)

130. Paragraphs 1 to 129 are incorporated herein as set forth above.

131. Zydus has committed an act of infringement of the ’296 Patent that creates a justiciable case or controversy between Takeda and Zydus.

132. Zydus’s submission of its ANDA No. 211519 to seek approval to engage in the commercial use, manufacture, sale, offer for sale, or importation of Zydus’s ANDA Product prior to expiration of the ’296 Patent constitutes infringement of one or more claims of the ’296 Patent, including at least claim 1 of the ’296 Patent under 35 U.S.C. § 271(e)(2)(A).

133. Unless enjoined by the Court, upon FDA approval of ANDA No. 211519, Zydus will induce infringement of the ’296 Patent under 35 U.S.C. § 271(b) by making, using, importing, selling, and offering to sell Zydus’s ANDA Product in the United States. On information and belief, upon approval of ANDA No. 211519, Zydus will intentionally encourage acts of direct infringement by healthcare providers administering, and/or patients using, Zydus’s ANDA Product with knowledge of the ’296 Patent and knowledge that its acts are encouraging infringement.

134. Takeda will be irreparably harmed by Zydus’s infringing activities unless those activities are enjoined by this Court.

135. Takeda does not have an adequate remedy at law.

COUNT XIII

(Infringement of the ’655 Patent)

136. Paragraphs 1 to 135 are incorporated herein as set forth above.

137. Zydus has committed an act of infringement of the ’655 Patent that creates a justiciable case or controversy between Takeda and Zydus.

138. Zydus’s submission of its ANDA No. 211519 to seek approval to engage in the commercial use, manufacture, sale, offer for sale, or importation of Zydus’s ANDA Product prior to expiration of the ’655 Patent constitutes infringement of one or more claims of the ’655 Patent, including at least claim 1 of the ’655 Patent under 35 U.S.C. § 271(e)(2)(A).

139. Unless enjoined by the Court, upon FDA approval of ANDA No. 211519, Zydus will induce infringement of the ’655 Patent under 35 U.S.C. § 271(b) by making, using, importing, selling, and offering to sell Zydus’s ANDA Product in the United States. On information and belief, upon approval of ANDA No. 211519, Zydus will intentionally encourage acts of direct infringement by healthcare providers administering, and/or patients using, Zydus’s ANDA Product with knowledge of the ’655 Patent and knowledge that its acts are encouraging infringement.

140. Takeda will be irreparably harmed by Zydus’s infringing activities unless those activities are enjoined by this Court.

141. Takeda does not have an adequate remedy at law.

COUNT XIV

(Infringement of the ’395 Patent)

142. Paragraphs 1 to 141 are incorporated herein as set forth above.

143. Zydus has committed an act of infringement of the ’395 Patent that creates a justiciable case or controversy between Takeda and Zydus.

144. Zydus's submission of its ANDA No. 211519 to seek approval to engage in the commercial use, manufacture, sale, offer for sale, or importation of Zydus's ANDA Product prior to expiration of the '395 Patent constitutes infringement of one or more claims of the '395 Patent, including at least claim 1 of the '395 Patent under 35 U.S.C. § 271(e)(2)(A).

145. Unless enjoined by the Court, upon FDA approval of ANDA No. 211519, Zydus will induce infringement of the '395 Patent under 35 U.S.C. § 271(b) by making, using, importing, selling, and offering to sell Zydus's ANDA Product in the United States. On information and belief, upon approval of ANDA No. 211519, Zydus will intentionally encourage acts of direct infringement by healthcare providers administering, and/or patients using, Zydus's ANDA Product with knowledge of the '395 Patent and knowledge that its acts are encouraging infringement.

146. Takeda will be irreparably harmed by Zydus's infringing activities unless those activities are enjoined by this Court.

147. Takeda does not have an adequate remedy at law.

COUNT XV

(Infringement of the '396 Patent)

148. Paragraphs 1 to 147 are incorporated herein as set forth above.

149. Zydus has committed an act of infringement of the '396 Patent that creates a justiciable case or controversy between Takeda and Zydus.

150. Zydus's submission of its ANDA No. 211519 to seek approval to engage in the commercial use, manufacture, sale, offer for sale, or importation of Zydus's ANDA Product prior to expiration of the '396 Patent constitutes infringement of one or more claims of the '396 Patent, including at least claim 1 of the '396 Patent under 35 U.S.C. § 271(e)(2)(A).

151. Unless enjoined by the Court, upon FDA approval of ANDA No. 211519, Zydus will induce infringement of the ’396 Patent under 35 U.S.C. § 271(b) by making, using, importing, selling, and offering to sell Zydus’s ANDA Product in the United States. On information and belief, upon approval of ANDA No. 211519, Zydus will intentionally encourage acts of direct infringement by healthcare providers administering, and/or patients using, Zydus’s ANDA Product with knowledge of the ’396 Patent and knowledge that its acts are encouraging infringement.

152. Takeda will be irreparably harmed by Zydus’s infringing activities unless those activities are enjoined by this Court.

153. Takeda does not have an adequate remedy at law.

COUNT XVI

(Infringement of the ’721 Patent)

154. Paragraphs 1 to 153 are incorporated herein as set forth above.

155. Zydus has committed an act of infringement of the ’721 Patent that creates a justiciable case or controversy between Takeda and Zydus.

156. Zydus’s submission of its ANDA No. 211519 to seek approval to engage in the commercial use, manufacture, sale, offer for sale, or importation of Zydus’s ANDA Product prior to expiration of the ’721 Patent constitutes infringement of one or more claims of the ’721 Patent, including at least claim 1 of the ’721 Patent under 35 U.S.C. § 271(e)(2)(A).

157. Unless enjoined by the Court, upon FDA approval of ANDA No. 211519, Zydus will induce infringement of the ’721 Patent under 35 U.S.C. § 271(b) by making, using, importing, selling, and offering to sell Zydus’s ANDA Product in the United States. On information and belief, upon approval of ANDA No. 211519, Zydus will intentionally encourage acts of direct infringement by healthcare providers administering, and/or patients using, Zydus’s

ANDA Product with knowledge of the '721 Patent and knowledge that its acts are encouraging infringement.

158. Takeda will be irreparably harmed by Zydus's infringing activities unless those activities are enjoined by this Court.

159. Takeda does not have an adequate remedy at law.

COUNT XVII

(Infringement of the '722 Patent)

160. Paragraphs 1 to 159 are incorporated herein as set forth above.

161. Zydus has committed an act of infringement of the '722 Patent that creates a justiciable case or controversy between Takeda and Zydus.

162. Zydus's submission of its ANDA No. 211519 to seek approval to engage in the commercial use, manufacture, sale, offer for sale, or importation of Zydus's ANDA Product prior to expiration of the '722 Patent constitutes infringement of one or more claims of the '722 Patent, including at least claim 1 of the '722 Patent under 35 U.S.C. § 271(e)(2)(A).

163. Unless enjoined by the Court, upon FDA approval of ANDA No. 211519, Zydus will induce infringement of the '722 Patent under 35 U.S.C. § 271(b) by making, using, importing, selling, and offering to sell Zydus's ANDA Product in the United States. On information and belief, upon approval of ANDA No. 211519, Zydus will intentionally encourage acts of direct infringement by healthcare providers administering, and/or patients using, Zydus's ANDA Product with knowledge of the '722 Patent and knowledge that its acts are encouraging infringement.

164. Takeda will be irreparably harmed by Zydus's infringing activities unless those activities are enjoined by this Court.

165. Takeda does not have an adequate remedy at law.

PRAYER FOR RELIEF

WHEREFORE, Takeda requests entry of judgment in its favor and against Zydus as follows:

A. For a judgment and decree that Zydus has infringed one or more claims of Takeda's Colcrys® Patents under 35 U.S.C. § 271(e)(2)(A) by submitting its ANDA No. 211519 with a Paragraph IV Certification seeking approval to engage in the commercial use, manufacture, sale, offer for sale, or importation of Zydus's ANDA Product prior to the expiration of the Patents;

B. For a declaration that the commercial use, sale, offer for sale, manufacture, and/or importation by Zydus of its ANDA Product would infringe one of more claims of Takeda's Colcrys® Patents under 35 U.S.C. § 271(b);

C. For an order preliminarily and permanently enjoining Zydus and its affiliates, subsidiaries, directors, employees, agents, representatives, licensees, successors, assigns, and all other persons acting or attempting to act in active concert or participation with it or acting on its behalf, from infringing the Colcrys® Patents;

D. For an order that, if Zydus engages in the commercial manufacture, use, importation into the United States, sale, or offer for sale of its ANDA Product before the expiration of the Patents, a judgment be awarded to Takeda for damages resulting from such infringement, together with interest, in an amount to be determined at trial;

E. For an order pursuant to 35 U.S.C. 271(e)(4)(A) that the effective date for approval of ANDA No. 211519, under § 505(j) of the FFDCA (21 U.S.C. § 355(j)), be no earlier than the expiration date of the last of the Colcrys® Patents, including any extensions or adjustments;

F. For an order declaring this an exceptional case under 35 U.S.C. § 285, and awarding to Takeda its reasonable attorneys' fees, costs, and expenses; and

G. For such other and further relief as this Court deems just and proper.

Respectfully submitted,

Date: March 28, 2018

MCCARTER & ENGLISH, LLP

s/ John E. Flaherty

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CERTIFICATION PURSUANT TO LOCAL CIVIL RULE 11.2

Pursuant to Local Civil Rule 11.2, Plaintiff hereby certifies that the matter in controversy is related to the subject matter of the following actions:

- *Takeda Pharmaceuticals U.S.A., Inc. v. Zydus Pharmaceuticals (USA), Inc. and Cadila Healthcare Limited*, Civil Action No. 1:18-cv-00464 (D. Del.);
- *Takeda Pharmaceuticals U.S.A. Inc. v. Par Pharmaceutical Inc.*, Civil Action No. 1:12-cv-00419-SLR (D. Del.);
- *Takeda Pharmaceuticals USA Inc. v. Par Pharmaceutical Companies Inc. and Par Pharmaceutical Inc.*, Civil Action No. 1:13-cv-01524-SLR (D. Del.);
- *Takeda Pharmaceuticals USA Inc. v. Amneal Pharmaceuticals LLC*, Civil Action No. 1:13-cv-01729-SLR (D. Del.);
- *Takeda Pharmaceuticals USA Inc. v. Watson Laboratories Inc.*, Civil Action No. 1:14-cv-00268-SLR (D. Del.);
- *Takeda Pharmaceuticals U.S.A., Inc. v. Hikma Americas Inc., Hikma Pharmaceuticals PLC, and West-Ward Pharmaceutical Corporation*, Civil Action No. 1:14-cv-01268-RGA (D. Del.);
- *Takeda Pharmaceuticals U.S.A., Inc. v. Mylan Pharmaceuticals Inc.*, Civil Action No. 1:16-cv-00987-RGA (D. Del.);
- *Takeda Pharmaceuticals U.S.A., Inc. v. Mylan Pharmaceuticals Inc.*, Civil Action No. 1:16-cv-00202-IMK (N.D. W. Va.);
- *Takeda Pharmaceuticals U.S.A., Inc. v. Granules Pharmaceuticals Inc.*, Civil Action No. 1:17-cv-01019-RGA (D. Del.);
- *Takeda Pharmaceuticals U.S.A., Inc. v. Hetero Labs Limited, Hetero Labs Limited Unit-V and Hetero USA Inc.*, Civil Action No. 1:17-cv-01020-RGA (D. Del.);
- *Takeda Pharmaceuticals U.S.A., Inc. v. Macleods Pharmaceuticals LTD. and Macleods Pharma USA, Inc*., Civil Action No. 1:17-cv-01469-RGA (D. Del.);
- *Takeda Pharmaceuticals U.S.A., Inc. v. Strides Pharma Global PTE Limited and Strides Pharma Inc.*, Civil Action No. 1:17-cv-01690-RGA (D. Del.);
- *Takeda Pharmaceuticals U.S.A., Inc. v. Dr. Reddy's Laboratories, Ltd. and Dr. Reddy's Laboratories, Inc.*, Civil Action No. 1:18-cv-00101-RGA (D. Del.); and

- *Takeda Pharmaceuticals U.S.A., Inc. v. Alkem Laboratories Limited and Ascend Laboratories, LLC*, Civil Action No. 18-0189 (D. Del.).

Respectfully submitted,

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